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Rapid determination of the reaction kinetics of an n-butylbenzaldimine synthesis using a novel mesoscale oscillatory baffled reactor

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Abstract

Two designs of "mesoscale" (~4-5 mm diameter) oscillatory baffled reactor (OBR), namely integral (orifice plate-type) and central (axial disc) baffled OBRs were developed and characterised at low net flow rates of 0.4 – 1.0 ml/min (corresponding to $1.6 \leq Re_n \leq 5.0$) over a wide range of oscillation conditions of $80 \leq Re_o \leq 200$. For a reactor volume of approximately 30 ml and residence times from 25 to 90 min, high degrees of plug flow were achieved. For the integral design, the maximum number of tanks-in-series (N) achieved was 30 at Re_o=130. Using the centrally baffled design, the maximum number of tanks-in-series achieved was 40, at $Re_o \geq 180$ for $Re_n \geq 4$. As plug flow can be easily achieved over a wide operating window at very low flow rates, these novel designs are ideal for rapid continuous process screening at laboratory scale. The reaction of benzaldehyde with n-butylamine to form the imine was chosen to demonstrate the ability of the mesoscale OBRs to rapidly screen process conditions and obtain kinetic data. *In situ* FTIR spectroscopy was used to determine concentrations in real time. The relative flows of the reagents were controlled to impose successions of aldehyde:amine molar ratios. A clear step-change between these molar ratios was observed and the kinetics of the reaction were modelled and determined. The results showed that the rate constants were 1.9×10^{-2} s^{-1} and 2.0×10^{-2} s^{-1} for the beaker and the meso-OBR, respectively.

Keywords: Reaction kinetics; imine synthesis; benzaldehyde; n-butylamine; rate constant; schiff base formation; mesoscale OBR

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1. Introduction

The determination of reaction kinetics of systems is essential for determining chemical process mechanisms and sizing reactors. Traditionally, this is achieved in batch mode by monitoring the changing concentration of a reactant in a well-mixed vessel [1]. However, when batch vessels area scaled up, the heat and mass transfer can be limiting, and the same degree of mixing is usually unachievable.

Mesoscale Oscillatory Baffled Reactors ("mesoscale-OBRs") have similar periodic vortex patterns as conventional Oscillatory Baffled Reactors [2]. This has the advantages in energy requirement and mass transfer. For instance, energy saving was reported in a flocculation process, which only required an average shear rate of $13.1s^{-1}$ achieve 90% yield compared to $300s^{-1}$ in stirred tank [3]. A study on yeast re-suspension and culture showed that the mass transfer rate could be increased by ≥50% in an OBR compared to stirred tank reactors [4]. OBRs can be operated in batch or continuous mode depending on the purpose of the work [3, 5]. However, by conducting kinetic studies in flow parameters can be determined more rapidly.

The most typical form of mesoscale OBR consists of tubes of 350mm length and approximately 5.0 mm internal diameter. It is being developed as a platform to conduct process screening or preliminary feasibility studies at laboratory scale [6]. This "mesoscale" (diameters of mm) bridges the gap between micro- and macroscale systems, and this broadens the selection of laboratory or small-scale reaction analysis [7]. In addition, due to their small volume and because they provide plug flow at low flow rates, these reactors require very little feedstock and produce very small volumes of waste. This would be a particular advantage when very expensive reagents are required or hazardous wastes produced. Apart from that, this reactor in principle could be easily scaled-up, whilst maintaining its mixing behaviour and patterns.

Two types of baffle designs were developed. The integral baffles (Fig 1(a)) with smooth periodic constrictions allows low shear rate to be employed [2] and the centrally baffled design (Fig 1(b)) consists of hexagonal stainless steel solid discs placed along a narrow rod.

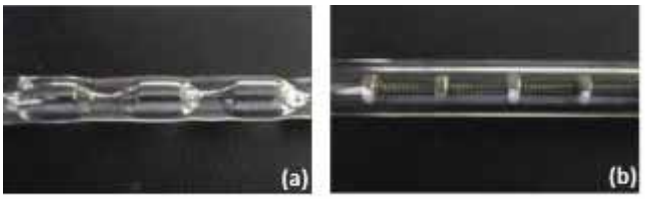


Fig. 1. Different types of baffled designs; (a) Integral baffles; (b) Central baffles

The flow patterns in these reactors are described by geometrical and dynamic parameters [8]. The geometrical parameters are the baffle spacing (L) and the baffle open area (S) as described below:

$$L = 1.5D \quad (1)$$

$$S = \frac{d_o^2}{D^2} \text{ (Typically in the range 0.2-0.4)} \quad (2)$$

…where d_o is the baffle diameter and D is the tube diameter

These parameters influence the size and shape of eddies generated in baffle cavities [9]. The dynamic parameters are the oscillatory Reynolds number (Re_o), net flow Reynolds number (Re_n), velocity ratio (Ψ) and Strouhal number (St):

$$Re_o = \frac{2\pi f x_o \rho D}{\mu} \tag{3}$$

$$\psi = Re_o / Re_n \tag{4}$$

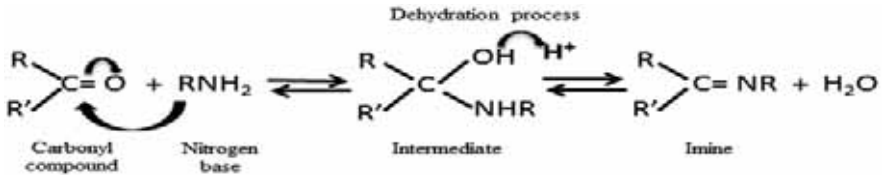
$$Re_n = \frac{\rho D u}{\mu} \tag{5}$$

$$St = \frac{D}{4\pi x_o} \tag{6}$$

…where u (m/s) is the superficial velocity; D (m) is the tube diameter; μ (m^2s^{-1}) is the viscosity; x_o (m) is oscillation amplitude (centre to peak); f (Hz) is the oscillation frequency and ρ (kg $m^{-3}s^{-1}$) is fluid density.

The oscillatory Reynolds number describes the intensity of the mixing applied inside the system. It is similar to Re_n, but the superficial velocity (u) is replaced by the maximum oscillatory velocity ($2\pi fx_o$). Velocity ratio (ψ) is the ratio of oscillatory flow and net flow which describes the interdependency of the Re_o and Re_n. The Strouhal number (St) describes the effectiveness of the eddy propagation in relation to the tube geometry, which is inversely proportional to the oscillation amplitude.

The objective of this work was to demonstrate the mesoscale-OBR as a tool for obtaining representative kinetic data of a chemical reaction. This is intended to reduce process development time significantly, by allowing optimal conditions to be determined rapidly and logically. Imination, as a single-phase reaction system, was identified as a good candidate. This reaction, also known as Schiff base formation, was chosen as a case study due to its simplicity and well-known kinetics and because it has several applications in biological processes, polymer synthesis and dynamic combinatorial chemistry [10-12]. The reaction is exothermic and reversible. Generally, the mechanism involves the nitrogen base attacking the carbonyl compound to form an intermediate addition substance, then follows dehydration steps to form an imine [13] as shown below:



(7)

This reaction has previously been monitored by several analytical methods such as Raman and Infrared Spectroscopy [14-15]. When using Raman, the determination was conducted offline, whereas real-time measurement was performed using FTIR. In both cases the reaction was studied in batch. In this work, *in situ* FTIR was used to monitor real-time quantitative and qualitative characteristics of the reaction system.

Nomenclature

D	tube internal diameter (m)
d_o	baffled diameter (m)
f	oscillation frequency (Hz)
L	baffled spacing
N	number of tank-in-series
Re_n	net flow Reynolds number
Re_o	oscillatory Reynolds number
S	baffle open area
St	Strouhal number
t_i	time (s)
u	superficial velocity (m/s)
x_o	centre to peak amplitude of oscillation (m)
ψ	velocity ratio
μ	viscosity (m^2s^{-1})
ρ	fluid density (kg $m^{-3}s^{-1}$)
θ	dimensionless time
τ	residence time

2. Apparatus and experimental procedure

2.1. Residence time distribution (RTD) experiment

The experimental set-up for the residence time distribution (RTD) analysis is shown in Fig 2. Three PVM Confluent syringe pumps (Eurodyne Ltd) were used to provide net flow (water was used in this case), inject the tracer and oscillate the fluid. Prior to experiments, the pump system and reactor must be air-free. The pumps were set to the desired oscillation condition (frequency and amplitude) and net flow (Re_n). The oscillation conditions were manipulated through the piston movement, with the frequency of the oscillation controlled by the speed of the piston, and the oscillation amplitude by the amount of liquid dispensed.

Approximately 0.5 ml of 3.0M potassium chloride (KCl) tracer was injected at the highest flowrate (1800 ml/hr) to obtain a pulse injection. At the outlet, the conductivity was measured using a 4mm diameter E61014 probe connected to a CDM210 conductivity meter (Hach-Lange Ltd). This

measurement was carried on until the conductivity was zero . The data was recorded using a Picolog recorder.

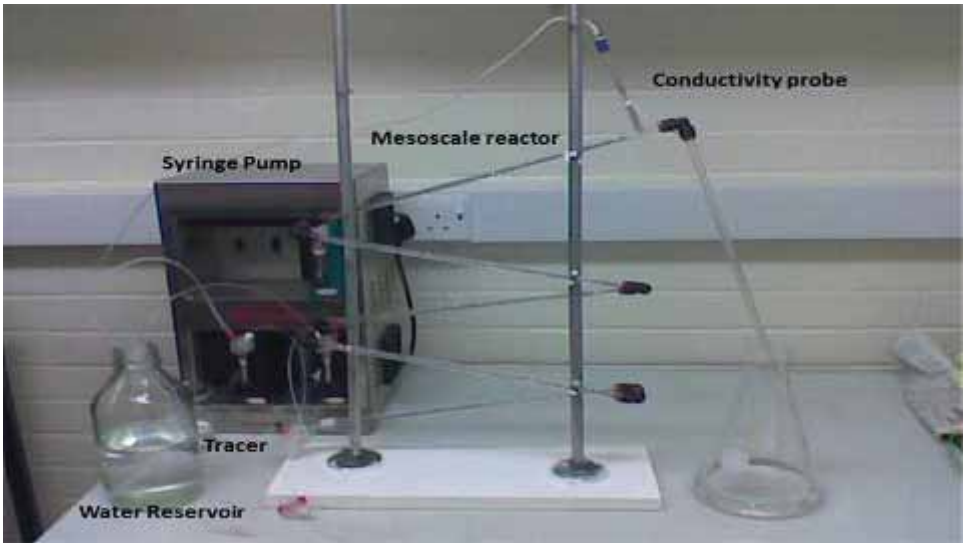


Fig. 2. Experimental set-up for RTD analysis for mesoscale OBR

RTD was quantified using the tank- in- series (N) model with the assumption that each baffle cavity of the mesoscale OBR act as a single tank. The model was used because of its simplicity and flexibility yet effective model[16]. The variables were performed in its dimensionless forms to normalize the data as follows:

$$\textit{Dimensionless time: } \theta = \frac{t_i}{\tau} \tag{9}$$

where

$$\textit{Mean residence time: } \tau = \frac{\sum_i t_i C_i \Delta t_i}{\sum_i C_i \Delta t_i} \tag{10}$$

C_i the existing tracer concentration at time t_i and Δt_i is the interval between two measurements

$$\textit{Distribution curve: } E(\theta) = \tau \left(C_i / \Delta_i C_i \Delta t_i\right) \tag{11}$$

$$\textit{Variance: } \sigma(\theta)^2 = \Sigma_i \left[(\theta-1)^2 E(\theta) \Delta\theta\right] \tag{12}$$

$$N = \frac{1}{\sigma(\theta)^2} \tag{13}$$

In order to approach the RTD Gaussion form curve, the value of the tank-in-series should be N≥10 and variance (σ^2) value indicate a plug flow at zero and infinity for pure laminar flow [16-17].

2.2. Imine synthesis

Kinetic measurements were carried out at ambient temperature (25^{o}C) and pressure. The consumption of benzaldehyde was used to determine the kinetics and mechanism of the imination reaction by monitoring the peak at 1714cm^{-1} region which is due to the C=O structure of the benzaldehyde. The FTIR spectra were recorded in the absorbance mode from 4000 to 650cm^{-1} at a resolution of 8cm^{-1}.

The chemicals used in this research were: benzaldehyde (C_7H_5O), n-butylamine ($C_4H_{11}N$) and hexane (C_6H_{14}). All these reactants were of analytical grade, purchased from Sigma-Aldrich with purification percentage of >98%.

2.2.1. Reaction with mesoscale-OBR

The experimental set-up for the imine synthesis using mesoscale OBR with central baffle is shown in Fig 3. Three syringe pumps (Eurodyne Ltd) were used to provide net flows and oscillate the reaction mixture. The IR probe was immersed at the end of the of the reactor. For batch reaction, amine and aldehyde were dispensed into a mesoreactor at the same flow rate of 1800ml/hr until the total volume reached 6 mL. Immediately after this step, the spectra of the reaction were taken *in situ* at intervals of 15 seconds for 60 minutes. This process was carried out at oscillatory Reynolds numbers between 35 and 400.

The flow reactions were carried out at the same condtions, but the flow rate was accordingly adjusted to the residence time required.

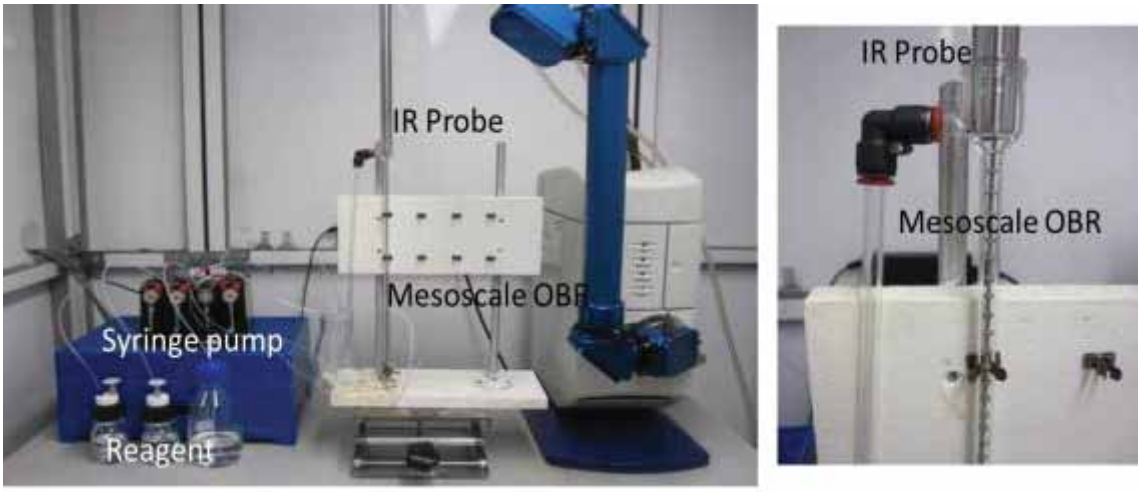


Fig. 3. Experimental set-up for imine synthesis using mesoscale-OBR

2.2.2. Reaction with beaker

A batch reaction of the imine synthesis was conducted using a 100 mL volume beaker for comparison. Each reagent (amine and aldehyde) of 40 mL were added into the beaker and vigorously stirred using a magnetic stirrer. The spectra of the reaction were also taken *in-situ* at an interval of 15 seconds for 60 minutes by immersing the IR probe at the middle of the beaker. The process was repeated with different speeds from 200rpm – 1200rpm.

3. Results and Discussion

3.1. Establishing plug flow behaviour

The plug flow behaviour of the mesoscale OBR at 10-15 min residence time was characterised over a wide range of net flow Reynolds numbers (1 - 34) and oscillatory Reynolds numbers of 50-500 (x_o=0.5-4mm and *f*:0.5-10Hz), well-established elsewhere [6]. The RTD, characterized as the number of tanks-in-series (N), was determined for all three baffle designs at various net flows ($1.56 \leq Re_n \leq 4.67$) and oscillation conditions ($40 \leq Re_o \leq 650$). The net flow (Re_n) imposed provided equivalent residence times from 25-90 min.

3.1.1 The integral baffle design

The interaction of the Re_n and Re_o for the integral design can be observed in Fig 4, below. The number of tanks-in-series (N) broadly decreases with increasing oscillatory Reynolds number (Re_o). Between Re_n=1.56 and 3.11, the reduction in the number of tank-in-series (N) was about 10%. This can be observed at Re_o=125 and 180, where N decreased significantly e.g. from ~20 to 10 tanks for Re_n = 1.56.

Regardless of the tested range of net flows (Re_n=1.56, 3.11 and 4.67), the lowest number of tanks-in-series (N=15) was always observed at St=0.2 (x_o=2mm). This shows that the integrally baffled mesoscale OBR should be operated at St≥0.2 to ensure optimum plug flow behaviour. At smaller value of St (St≤0.2), the size of eddies generated is bigger. Here, the vortices tend to propagate into adjacent baffle cavities, thereby creating axial dispersion of the pulse, reducing the number of theoretical stirred tanks.

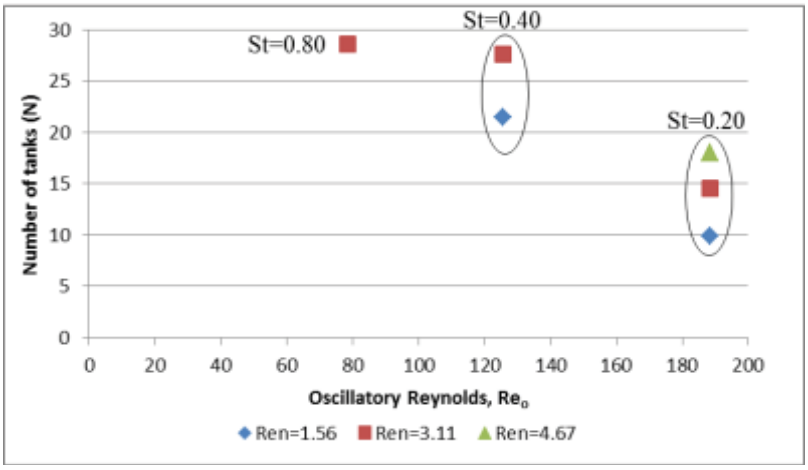


Fig. 4. Dependence of RTD performances on oscillation reynolds number (Re_o) for integral baffles

3.1.2 The central baffle design

The centrally baffled design exhibited two distinctive trends (Fig 5). Firstly, at $Re_n \geq 4$ the maximum N was achieved at higher oscillation condition ($Re_o \geq 180$) e.g for $Re_o=190$, N was approximately 40 for $Re_n=4.39$ and 4.67. The opposite effect was observed at $Re_n < 4$ which only required oscillation condition in the region of $Re_o=130$ to achieve a high degree of plug flow.

For all Re_ns used, the degree of plug flow decreased with increasing St. This can be observed, e.g for $Re_n=2.19$ where the N decreases from 50 to 25 at St of 0.2 and 0.4 respectively. This shows that lower values of St (higher amplitude), which produce larger vorteices are required for the radial mixing to become significant.

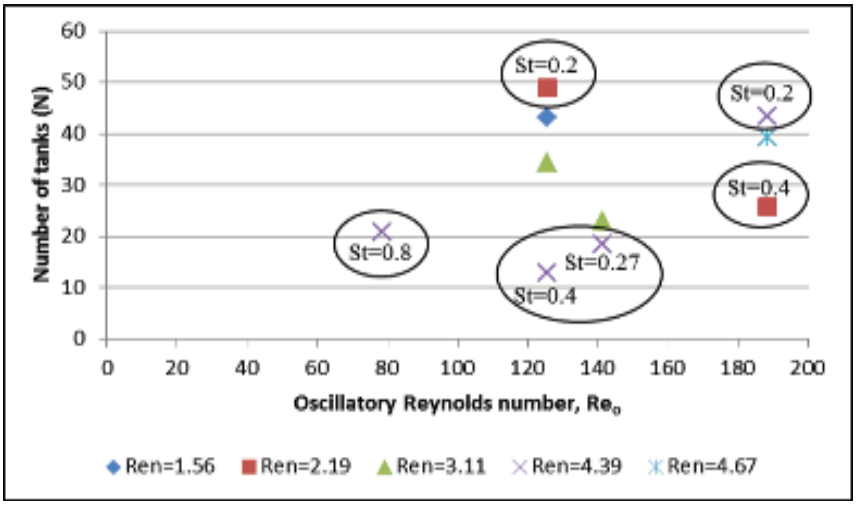


Fig. 5. Dependence of RTD performances on oscillation reynolds number (Re_o) for central baffles

3.1.3. Baffle design summary

Overall, the RTD data showed that mesoscale OBRs can produce plug flow over a wide range of net flow conditions. This has an important advantage in screening chemical reactions, as it allows processes to be studied at residence times ranging from seconds to hours.

For the imine kinetics investigated here, central baffles were used because they provide higher degrees of plug flow behaviour than the integral baffles of the desired conditions (e.g at $Re_n=3.11$ and $Re_o=120$, N was 35 with centrally baffles compared to N=28 with integral design). Furthermore, the centrally baffled design was developed to provide higher shear mixing than the integral design, as the baffles are sharper-edged.

3.2. Batch system reaction kinetics investigation

The imine synthesis performed using the centrally baffled mesoscale OBR design (Fig 6(a)) and beaker (Fig 6(b)) in batch mode to determine kinetics parameters, e.g. rate constant show comparable results.

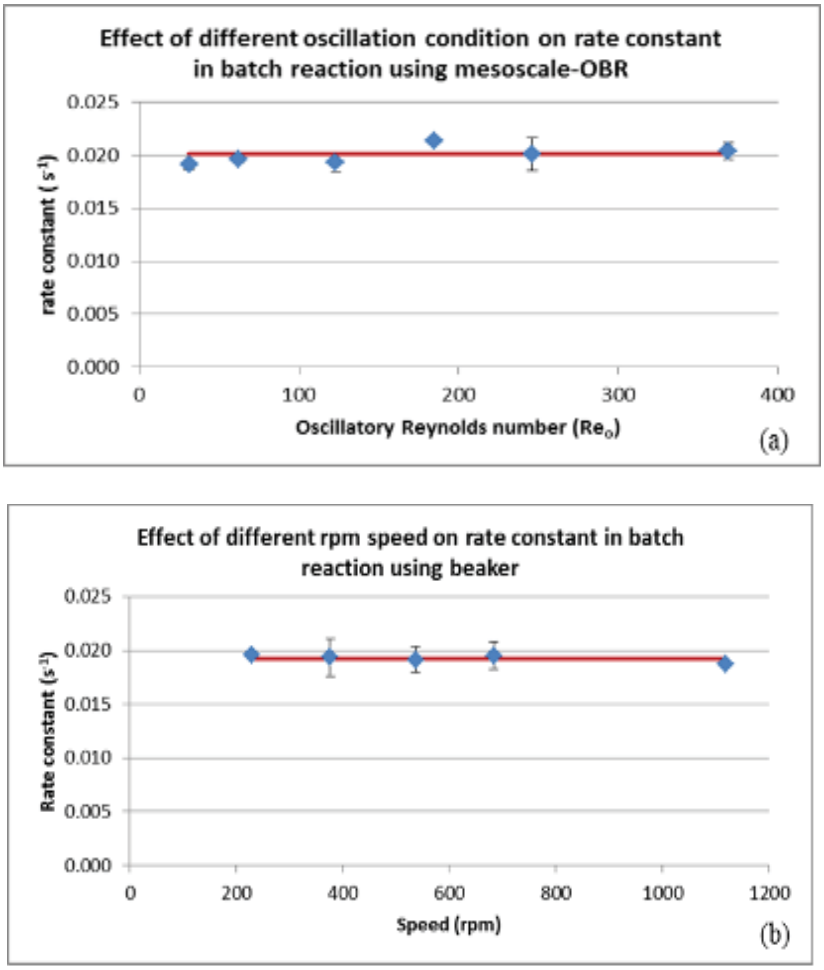


Fig. 6. Rate constant of imine synthesis using (a) mesoscale-OBR with central baffle design and (b) 100 ml beaker

The average rate constant was 1.9 x 10^{-2} s^{-1}±0.001 and 2.0 x 10^{-2} s^{-1}±0.0006 for the beaker and mesoscale OBR respectively. However, the mesoscale OBR data exhibited higher reproducibility, as its average standard deviation was 7.1 x 10^{-4} s^{-1}, compared to 9.1 x 10^{-4} s^{-1} for the beaker (see Table 1 below).

Table 1. Comparison of standard deviation of rate constant using different reaction vessel.

Beaker		Mesoscale OBR	
Rpm	**Standard deviation**	**Re_o**	**Standard deviation**
229	2.1×10^{-4}	31	4.2×10^{-4}
337	1.8×10^{-2}	62	3.5×10^{-4}
537	1.2×10^{-3}	123	9.2×10^{-4}
684	1.3×10^{-3}	185	2.1×10^{-4}
1119	7.1×10^{-5}	246	1.6×10^{-3}
		369	7.8×10^{-4}

3.3. Flow system in reaction kinetics investigation

From the RTD study (section 3.1); the plug flow for the centrally baffled mesoreactor design can be achieved at amplitudes (x_o) below 2.0 mm and frequencies (f) of any value in the range of 0.5 – 4.0 Hz for $Re_n \geq 4.0$. As can be observed in Fig 7 below, a clear step-change from the ratio of aldehyde:amine of 1:1 to 1:2 was obtained at oscillation condition (1mm amplitude and 1Hz frequency) in which plug flow behaviour was achieved. In contrast, a sharp change in the outlet concentration is not apparent at the poor plug flow condition of 4mm amplitude and 3 Hz.

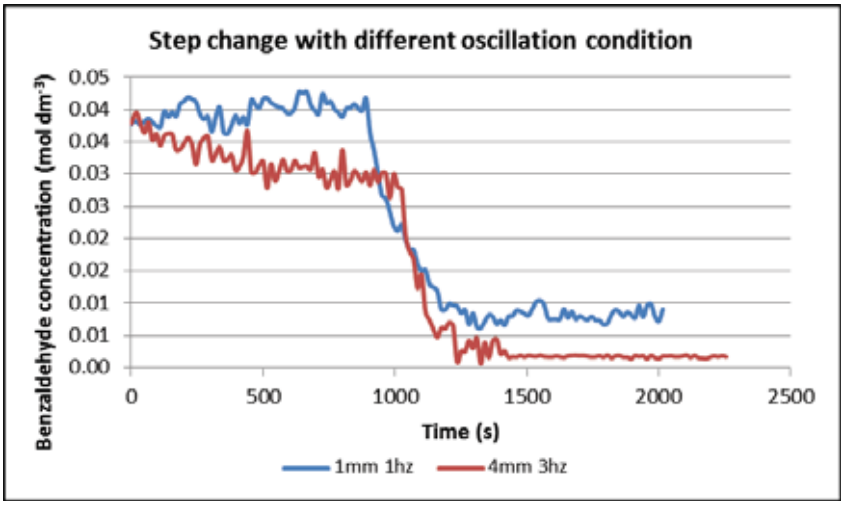


Fig. 7. Comparison of steady state condition at plug flow (1 mm 1 Hz) and non-plug flow condition (4 mm 3 Hz) using central baffle design mesoscale OBR.

The imine synthesis was conducted over various residence times at equal concentration of both reactants (benzaldehyde and n-butylamine) in flow. Under these operating conditions, a clear step-change between residence times was observed (Fig 8). This demonstrates how quickly and simply the parameter space can be screened using continuous reactors. Average data at each step were plotted and compared to the reduction profile of benzaldehyde in batch mode (Fig 9).

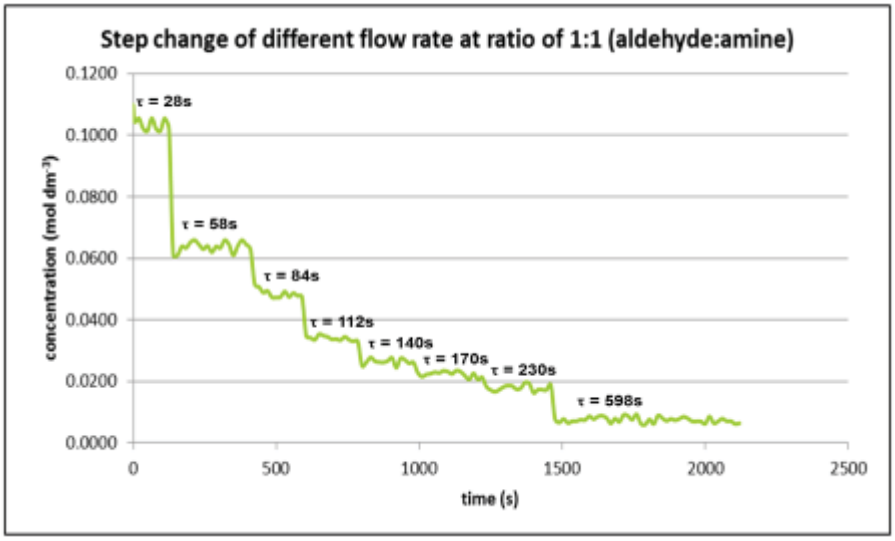


Fig. 8. Steady state step change of equal reaction of imine synthesis at plug flow condition with oscillation condition of 1mm 1Hz using central baffle design mesoscale OBR.

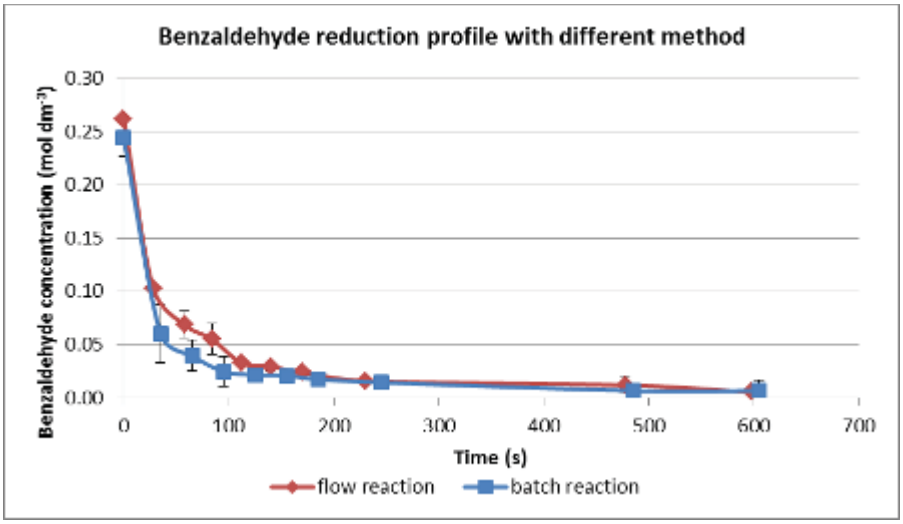


Fig. 9. Comparison of benzaldehyde reduction profile using different reaction kinetics investigation method at 1mm 1Hz oscillation condition for flow and 684rpm stirrer speed for batch.

The rate constant for the continuous mode was calculated using integration method develop for reaction in flow manner [1]. The model obtained by equating the rate of entry and removal of reactant from the system. The results of both, the continuous and batch mode results agreed extremely well, as shown in Table 2, below. A further advantage of using the continuous reactor can also be seen in Table 2: that it gave more consistent results than the batch with reproducibility of $5.0x10^{-4}$. The error was significantly lower (~50% that of the batch data):

The process development time using this continuous screening mesoscale OBR would be reduced by up to 50% compared to batch screening. Furthermore, the amount of reagent required would be reduced by 75% due to the small volume of the mesoscale reactor. Each steady state is equivalent to numerous batch reactions, as each element of fluid emerging can be thought of as one of these batch reactors. The only limitations to the number is the speed of analysis, here limiting the data frequency to one per 15s i.e. equivalent to a number of batch reactors equal to the duration of the steady state in seconds divided by 15.

Table 2. Rate constant of imine synthesis using different reaction kinetics investigation method

Method	Regression (R^2)	Rate Constant
Batch	0.93	0.019 ±0.0010
Flow	0.94	0.021±0.0005

4. Conclusion

Mesoscale OBRs can provide plug flow behaviour at low flowrates ($Re_n \leq 5$). This allows reaction systems to be investigated at residence times from a few seconds to up to a few hours in the same equipment: typically bench-scale reactors of footprint ~ 0.1 m^2. The mesoscale OBR system used here was able to screen reactions (i.e. exhibited a high degree of plug flow) at residence times between 10 and 90 min. When determining reaction kinetics in continuous reactors, plug flow is necessary so that changes between steady states can be clearly observed.

Here, the reaction of benzaldehyde with N-butylamine to form the imine was chosen to demonstrate the ability of the mesoscale OBRs to rapidly screen process conditions and obtain kinetic data. In situ FTIR spectroscopy was used to determine concentrations in real time. The rate constants were determined to be 1.9×10^{-2} s^{-1} and 2.0×10^{-2} s^{-1} for the beaker and the meso-OBR, respectively. Clearly, they agree very well. However, there were a number of advantages of using the mesoreactor system:

- the amount of reagant required for determining the rate constants was reduced by 75%
- the process development time was reduced by about 50% (compared to the batch reaction using beaker)
- the rate constant data gathered from the mesoscale system was more reproducible, with a standard deviation of 7.1×10^{-4} s^{-1}, compared to 9.1×10^{-4} s^{-1} for beaker

Acknowledgements

Financial support from the Malaysian Rubber Board (MRB) is gratefully acknowledged.

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